



PTO/SB/08a/b (07-08)

Approved for use through 09/30/2006. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/681,627-Conf. #7408
				Filing Date	October 8, 2003
				First Named Inventor	Carl H. June
				Art Unit	1633
				Examiner Name	A. M. S. Wehbe
Sheet	1	of	1	Attorney Docket Number	WYS-014.02

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Country Code <sup>4</sup> -Number-Kind Code <sup>5</sup> (if known)				

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
ML	CA	Augustine J. A. <i>et al.</i> , "Interleukin 2- and Polymavirus Middle T Antigen-Induced Modification of Phosphatidylinositol 3-Kinase Activity in Activated T Lymphocytes." <i>Molecular and Cellular Biology</i> , 1991, Vol. 11, No.9, p. 4431-4440.			
	CB	Davies A. A. <i>et al.</i> , "The Human T3y Chain Is Phosphorylated at Serine 126 in Response to T Lymphocyte Activation." <i>The Journal of Biological Chemistry</i> , 1987, Vol. 262, No. 23, p.10918-10921.			
	CC	Graber M. <i>et al.</i> , "The Protein Tyrosine Kinase Inhibitor Herbimycin A, but not Genistein, Specifically Inhibits Signal Transduction by the T Cell Antigen Receptor." <i>International Immunology</i> , 1992, Vol. 4, No. 11, p. 1201-1210.			
	CD	June C. H. <i>et al.</i> , "Inhibition of Tyrosine Phosphorylation Prevents T-cell Receptor Mediated Signal Transduction." <i>Proc. Natl Acad. Sci. USA</i> , 1990, Vol. 87, p. 7722-7726.			
	CE	Merida I. <i>et al.</i> , "IL-2 Binding Activates a Tyrosine-Phosphorylated Phosphatidylinositol-3-Kinase." <i>The Journal of Immunology</i> , 1991, Vol. 147, p. 2202-2207.			
	CF	Prasad K. V. S. <i>et al.</i> , "T-cell Antigen CD28 Interacts with the Lipid Kinase Phosphatidylinositol 3-kinase by a Cytoplasmic Tyr(P)-Met-Xaa-Met Motif." <i>Proc. Natl. Acad. Sci. USA</i> , 1994, Vol. 91, p. 2834-2838.			
	CG	Reif K. <i>et al.</i> , "Divergent Regulation of Phosphatidylinositol 3-Kinase P85α and P85β Isoforms upon T Cell Activation." <i>The Journal of Biological Chemistry</i> , 1993, Vol. 268, No. 15, p. 10780-10788.			
	CH	Shibasaki F. <i>et al.</i> , "Different Properties of Monomer and Heterodimer Forms of Phosphatidylinositol 3-kinases." <i>Biochem. J.</i> , 1993, Vol. 289, p. 227-231.			
	CI	Thompson P. A. <i>et al.</i> , "Identification of Distinct Populations of PI-3 Kinase Activity Following T-Cell Activation." <i>Oncogene</i> , 1992, Vol. 7, p. 719-725.			
	CJ	Torimoto, T. <i>et al.</i> , "CD45 Molecule and T Cell Activation." 1990. Vol. 27, p. 63-71.			
	CK	Vlahos C. J. <i>et al.</i> , "A Specific Inhibitor of Phosphatidylinositol 3-Kinase, 2-(4-Morpholinyl)-8-phenyl-4H-1-benzopyran-4-one (LY294002)." <i>The Journal of Biological Chemistry</i> , 1994, Vol. 269, No. 7, p. 5241-5248.			
	CL	Woscholski R. <i>et al.</i> , "A Comparison Of Demthoxyviridin And Wortmannin As Inhibitors Of Phosphatidylinositol 3-Kinase." <i>FEBS Letters</i> , 1994, Vol.342, p. 109-114.			

Examiner Signature	/Maria Leavitt/	Date Considered	12/19/2006
-----------------------	-----------------	--------------------	------------

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO. <b>RPI-015DV</b>	SERIAL NO. <b>10/681627</b>
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT <b>June, Carl H.</b>	
		FILING DATE <b>October 8, 2003</b>	GROUP <b>1632</b>

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
ML	A1	5,504,103	04/96	Bonjouklian <i>et al.</i>	514	453

## FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
ML A2	WO 90/05541	05/90	PCT		

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

ML	A3	Abe, R. <i>et al.</i> , "T Cell Receptor-mediated Recognition of Self-Ligand Induces Signaling in Immature Thymocytes before Negative Selection" <i>J. Exp. Med.</i> , Vol. 176, pp. 459-468, August 1992;
	A4	Baggiolini, M. <i>et al.</i> , "Inhibition of the Phagocytosis-Induced Respiratory Burst by the Fungal Metabolite Wortmannin and Some Analogues" <i>Experimental Cell Research</i> , Vol. 169, pp. 408-418, 1987;
	A5	Blunden, G. <i>et al.</i> , "Mycotoxins in food" <i>Medical Laboratory Sciences</i> , Vol. 48, pp. 271-282, 1991;
	A6	Closse, A. <i>et al.</i> , "2,3-Dihydrobenzofuran-2-ones: A New Class of Highly Potent Antiinflammatory Agents" <i>J. Med. Chem.</i> , Vol. 24, pp. 1465-1471, 1981;
	A7	Gunther, R. <i>et al.</i> , "Acute Pathological Effects on Rats of Orally Administered Wortmannin-Containing Preparations and Purified Wortmannin from <i>Fusarium Oxysporum</i> " <i>Fd. Chem. Toxic.</i> , Vol. 27, No. 3, pp. 173-179, 1989;
	A8	Gunther, R. <i>et al.</i> , "Immunosuppressive Effects of Dietary Wortmannin on Rats and Mice" <i>Immunopharmacology and Immunotoxicology</i> , Vol. 11, No. 4, pp. 559-570, 1989;
	A9	Harding, F.K. <i>et al.</i> , "CD28-mediated signalling co-stimulates murine T cells and prevents induction of anergy in T-cell clones" <i>Nature</i> , Vol. 356, pp. 607-609, 16 April 1992;
	A10	June, C.H., "Signal transduction in T cells" <i>Current Opinion in Immunology</i> , Vol. 3, pp. 287-293, 1991;
	A11	June, C.H. <i>et al.</i> , "Evidence for the Involvement of Three Distinct Signals in the Induction of IL-2 Gene Expression in Human T Lymphocytes" <i>J. Immunol.</i> , Vol. 143, No. 1, pp. 153-161, 1 July 1989;
	A12	June, C.H. <i>et al.</i> , "Role of the CD28 receptor in T-cell activation" <i>Immunology Today</i> , Vol. 11, No. 6, pp. 211-216, 1990;
	A13	Ledbetter, J.A. <i>et al.</i> , "CD28 Ligation in T-Cell Activation: Evidence for Two Signal Transduction Pathways" <i>Blood</i> , Vol. 75, No. 1, pp. 1531-1539, 1 April 1990;
✓	A14	Ledbetter, J.A. <i>et al.</i> , "Crosslinking of surface antigens cause mobilization of intracellular ionized calcium in T lymphocytes" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 84, pp. 1384-1388, March 1987;

Examiner

/Maria Leavitt/

Date Considered

12/18/2006

\*EXAMINER:

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

APPLICANT FACSIMILE OF FORM PTO-1449  
REV 7-00U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY DOCKET NO.

SERIAL NO.

RPI-015DV

10/681627

APPLICANT

June, Carl H.

FILING DATE

October 8, 2003

GROUP

1632

## LIST OF PUBLICATIONS CITED BY APPLICANT

(Use several sheets if necessary)

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.), Continued

			Lee, K. <i>et al.</i> , "The CD28 Signal Transduction Pathway in T Cell Activation" in <i>Advances of Cell Regulation of Cell Growth, Volume 2 - Cell Activation: Genetic Approaches</i> , J.J. Mond <i>et al.</i> (eds.), New York: Raven Press, Ltd., pp. 141-160, 1991;
	B2		Ley, S.C. <i>et al.</i> , "The T cell receptor/CD3 complex and CD2 stimulate the tyrosine phosphorylation of indistinguishable patterns of polypeptides in the human T leukemic cell line Jurkat" <i>Eur. J. Immunol.</i> , Vol. 21, pp. 2203-2209, 1991;
	B3		Lu, Yiling <i>et al.</i> , "CD28-Induced T Cell Activation: Evidence for a Protein-Tyrosine Kinase Signal Transduction Pathway" <i>J. Immunol.</i> , Vol. 149, No. 1, pp. 24-29, 1 July 1992;
	B4		Nunes, J. <i>et al.</i> , "Signalling through CD28 T-cell activation pathway involves an inositol phospholipid-specific phospholipase C activity" <i>Biochem. J.</i> , Vol. 293, pp. 835-842, 1993;
	B5		Okada, T. <i>et al.</i> , "Blockage of Chemotactic Peptide-induced Stimulation of Neutrophils by Wortmannin as a Result of Selective Inhibition of Phosphatidylinositol 3-Kinase" <i>J. Biol. Chem.</i> , Vol. 269, No. 5, pp. 3562-3567, 4 February 1994;
	B6		Okada, T. <i>et al.</i> , "Essential Role of Phosphatidylinositol 3-Kinase in Insulin-induced Glucose Transport and Antilipolysis in Rat Adipocytes" <i>J. Biol. Chem.</i> , Vol. 269, No. 5, pp. 3568-3573, 4 February 1994;
	B7		O'Shea, J.J. <i>et al.</i> , "Activation of human peripheral blood T lymphocytes by pharmacological induction of protein-tyrosine phosphorylation" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 89, pp. 10306-10310, November 1992;
	B8		Pérez-Blas, M. <i>et al.</i> , "Impaired T cell signal transduction through CD28 in a patient with idiopathic thrombocytopenia" <i>Clin. Exp. Immunol.</i> , Vol. 85, pp. 424-428, 1991;
	B9		Prasad, K.V.S., <i>et al.</i> , "Phosphatidylinositol (PI) 3-Kinase and PI 4-Kinase Binding to the CD4-p56 <sup>lck</sup> Complex: the p56 <sup>lck</sup> SH3 Domain Binds to PI 3-Kinase but Not PI 4-Kinase" <i>Molecular and Cellular Biology</i> , Vol. 13, No. 12, pp. 7708-7717, December 1993;
	B10		Prasad, K.V.S., <i>et al.</i> , "Src-homology 3 domain of protein kinase p59 <sup>lyn</sup> mediates binding phosphatidylinositol 3-kinase in T cells" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 7366-7370, August 1993;
	B11		Schwartz, A., <i>et al.</i> , "Quercetin Inhibition of the Induction and Fuction of Cytotoxic T Lymphocytes," <i>Immunopharmacology</i> , Vol. 4, pp. 125-138, 1982;
	B12		Schwartz, R.H., "A Cell Culture Model for T Lymphocyte Clonal Anergy" <i>Science</i> , Vol. 248, pp. 1349-1356, 15 June 1990;
	B13		Thompson, P.A., <i>et al.</i> , "Identification of distinct populations of PI-3 kinase activity following T-cell activation" <i>Oncogene</i> , Vol. 7, pp. 719-725, 1992;
	B14		Truitt, K.E. <i>et al.</i> , "Stimulation of CD28 Triggers an Association between CD28 and Phosphatidylinositol 3-Kinase in Jurkat T Cells" <i>J. Exp. Med.</i> , Vol. 179, pp. 1071-1076, March 1994;
	B15		Vandenberghe, P. <i>et al.</i> , "Antibody and B7/BB1-mediated Ligation of the CD28 Receptor Induces Tyrosine Phosphorylation in Human T Cells" <i>J. Exp. Med.</i> , Vol. 175, pp. 951-960, April 1992;
✓	B16		Ward, S.G. <i>et al.</i> , "Ligation of CD28 receptor by B7 induces formation of D-3 phosphoinositides in T lymphocytes independently of T cell receptor/CD3 activation" <i>Eur. J. Immunol.</i> , Vol. 23, pp. 2572-2577, 1993;

Examiner

/Maria Leavitt/

Date Considered

12/18/2006

\*EXAMINER:

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

APPLICANT FACSIMILE OF FORM PTO-1449  
REV 7-00U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY DOCKET NO.

SERIAL NO.

RPI-015DV

10/681627

LIST OF PUBLICATIONS CITED BY APPLICANT  
(Use several sheets if necessary)

APPLICANT

June, Carl H.

FILING DATE

October 8, 2003

GROUP

1632

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.), Continued

OTPE JC180 MAR 0 4 2004 PATENT & TRADEMARK OFFICE	C1	Ward, S.G. <i>et al.</i> , "Regulation of D-3 phosphoinositides during T cell activation via the T cell antigen receptor/CD3 complex and CD2 antigens" <i>Eur. J. Immunol.</i> , Vol. 22, pp. 45-49, 1992;
ML	C2	Ward, S.G. <i>et al.</i> , "Regulation of Phosphoinositide Kinases in T Cells" <i>J. Biol. Chem.</i> , Vol. 267, No. 33, pp. 23862-23869, 25 November 1992;
	C3	Ward, Stephen G. <i>et al.</i> "Inhibition of CD28-mediated T cell costimulation by the phosphoinositide 3-kinase inhibitor wortmannin" <i>Eur. J. Immunol.</i> Vol. 25, pp. 526-532, 1995;
	C4	Wiesinger, D. <i>et al.</i> , Antiinflammatory Activity of the New Mould Metabolite 11-Desacetoxy-Wortmannin and Some of its Derivatives" <i>Experientia</i> , Vol. 30, pp. 135-136, 1974;
	C5	Wu, W. and C.J. Mirocha, "Decreased Immunological Responses by Wortmannin-Containing Rice Culture of <i>Fusarium Oxysporum</i> and by Purified Wortmannin in Avian Species" <i>Immunopharmacology and Immunotoxicology</i> , Vol. 14, No. 4, pp. 913-923, 1992;
	C6	Wu, W. and Mirocha, C.J., "Wortmannin (A Mycotoxin) Inhibited Immune Responses in Chickens," <i>Poultry Science</i> , Vol. 71, suppl. 1, p. 13, 1992;
	C7	Yang, S.Y. <i>et al.</i> , "A Novel Activation Pathway for Mature Thymocytes" <i>J. Exp. Med.</i> , Vol. 168, pp. 1457-1468, October 1988;
	C8	Yano, H. <i>et al.</i> , "Inhibition of Histamine Secretion by Wortmannin through the Blockade of Phosphatidylinositol 3-Kinase in RBL-2H3 Cells" <i>J. Biol. Chem.</i> , Vol. 268, No. 34, pp. 25846-25856, 5 December 1993;
↓	C9	Yoshida, M., <i>et al.</i> , "Quercetin Arrests Human Leukemic T-Cells in Late G <sub>1</sub> Phase of the Cell Cycle," <i>Cancer Research</i> , Vol. 52, pp. 6676-6681, 1992.
Examiner	/Maria Leavitt/	
Date Considered	12/18/2006	
*EXAMINER:	Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	